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MORGAN, LEWIS & BOCKIUS LLP 1701 MARKET STREET PHILADELPHIA, PA 19103-2921			MYERS, CARLA J	
			ART UNIT	PAPER NUMBER
			1634	
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Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/036,645

Applicant(s)

BERD, DAVID

Examiner

Carla Myers

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 05 July 2006.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,2 and 21-33 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 2, and 21-33 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 5, 2006 has been entered.

Applicant's arguments set forth in the response of July 5, 2006 have been fully considered but are not persuasive to overcome all grounds of rejection. All rejections/objections not reiterated herein are hereby withdrawn.

Claims 1, 2, and 21-33 are pending and have been examined herein.

### **Improper Amendment**

2. The amendment filed July 5, 2006 does not comply with the requirements of 37 CFR 1.173(b), which sets forth the manner of making amendments in reissue applications. The amendment does not comply with 37 CFR 1.173(b)(2) because:

a) All subject matter being added to the patent must be underlined. In particular, the complete content of each of the newly added claims 21-31 (i.e., the claims that were not presented in the patent) should be underlined. It is noted that in the amendment of July 5, 2006, the content of claims 32 and 33 has been underlined, but the content of claims 21-31 is not underlined, as required by 37 CFR 1.173(b)(2).

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b) In claim 2, the phrase "wherein said vaccine induces delayed-type hypersensitivity (DTH) response against unmodified melanoma cells" has been added to the original patent claim and therefore should be underlined.

c) All subject matter being deleted from an original patent claim should be placed in brackets. In particular, in claim 1, the term "dinitrophenyl" has been deleted from the original patent claim and thereby should appear in brackets. Further, brackets and underlining are to be used to reflect only those changes in the text from the **original** patented claim, and **not** from any previous amendments in the reissue application. See 37 CFR 1.73(c). That is, in claim 1, the term "trinitrophenyl" which currently appears in brackets should be deleted and the term "dinitrophenyl" should be inserted therefor between the brackets. In claim 26, brackets should not be used (i.e. "[trinitrophenyl]" should be deleted) and the complete content of this claim should be underlined.

### ***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 26-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berd et al (Proceedings of the American Association for Cancer Research. March 1989. 30: page 382, abstract #1515) in view of Berd (Cancer Investigation. 1988. 6(3): 337-349; previously cited in IDS of U.S. Patent No. 5,290,551).

Berd (1989) teaches that treatment of melanoma patients with cyclophosphamide (CY) followed by autologous vaccine induces delayed-type hypersensitivity to melanoma cells and in some cases regression of metastatic cancer. To enhance this treatment, Berd studied the effectiveness of administering hapten conjugated autologous melanoma cells. The method of Berd comprises: (i) administering to a patient a low dose of cyclophosphamide; and (ii) 3 days following treatment with CY, injecting patients with a vaccine containing  $10\text{-}25 \times 10^6$  autologous, irradiated melanoma cells mixed with Bacille Calmette-Guerin (BCG). Berd reports that in a study of melanoma patients, one patient developed erythema and swelling in the dermal metastases on her leg and lower abdomen, followed by ulceration and drainage of necrotic material and some level of regression of the metastases. A second patient also showed erythema and swelling of the skin of her lower abdomen and groin and a change in consistency from rock-hard tumor to fluctuant. A third patient exhibited moderate erythema. All 3 patients developed delayed-type hypersensitivity (DTH) against both DNCB and DNP-conjugated autologous lymphocytes. Berd concluded that "(a)lthough the results are preliminary, they suggest that this new strategy may represent a significant advance in the immunotherapy of human melanoma."

While Berd (1989) teaches that the patients were injected with the DNP-conjugated melanoma vaccine, Berd does not specifically teach that the injection was intradermal, or that the injection was made to 3 sites on an upper arm or leg.

However, Berd (1988) teaches methods of immunotherapy for human melanoma wherein  $10\text{-}25 \times 10^6$  autologous melanoma cells mixed with BCG are injected

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intradermally into three sites on the patients upper arm or legs (see page 340, column 1). Berd reports that patients receiving CY and the melanoma vaccine developed DTH to tumor antigens (page 342, column 2). Three of the patients tested showed complete remission, one partial remission and two had minor responses to the vaccine (page 344, column 2).

According, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have practiced the method of Berd (1989) by injecting the DPN-conjugated melanoma vaccine mixed with BCG intradermally to 3 contiguous sites on the patient's upper arm or leg because as taught by Berd (1988) this is a conventional means for administering the melanoma cancer vaccine and would have provided an effective route of administration.

With respect to the recitation in the claims of "wherein administration of said vaccine induces a delayed-type hypersensitivity (DTH) response against unmodified melanoma cells" it is considered to be a property of the vaccine of Berd that it is capable of inducing a DTH response against unmodified melanoma cells. Given that the vaccine of Berd is identical to the vaccine of the present invention, in the absence of evidence to the contrary, the vaccine of Berd (1989) is expected to function similarly to the present vaccine. Therefore, the resulting method of intradermally injecting the DNP-vaccine of Berd (1989) would have necessarily resulted in a DTH response against unmodified melanoma cells.

With respect to claims 28 and 29, Berd (1989) does not characterize the melanoma patients that were treated with the DNP-conjugated melanoma vaccine and

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thereby does not specifically teach administering the vaccine to post-surgical melanoma patients or to stage 4 melanoma patients. However, Berd (1988; see, e.g., page 340) teaches administering melanoma vaccines to patients post-surgically and to patients with extensive metastatic disease. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have administered the DNP- conjugated melanoma vaccine of Berd (1989) to patients post-surgically and to stage 4 melanoma patients in order to have provided an effective means of treatment for those patients most in need of therapy.

With respect to claim 30, Berd (1989) teaches that of the four patients studied, three “developed a striking inflammatory response in tumor masses after 2 vaccine treatments (8 weeks).” Further, Berd (1988; page 340) teaches repeating the vaccine treatment every 28 days. The number of vaccine treatments ranged from 1 to 15, with a median of 4 treatments. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have intradermally administered the DNP-conjugated melanoma vaccine every 4 weeks because this would have boosted the response to the vaccine and thereby would have increased the effectiveness of the therapy.

With respect to claim 31, Berd (1989) does not teach that the autologous melanoma cells are cryopreserved. However, Berd (1988; page 340) teaches that the tumor masses are removed from the patient and tumor cells are cryopreserved in liquid nitrogen until needed. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used cryopreserved autologous

melanoma cells because this would have provided a more convenient means of administering the therapy since such cells could be frozen and stored and then administered at 4 week intervals.

4. Claims 26-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berd et al (Proceedings of the American Association for Cancer Research. March 1990. 31: page 279, abstract #1654) in view of Berd (1988).

Berd (1990) teaches a method of treating metastatic melanoma wherein the method comprises: (i) administering to a melanoma patient a low dose of cyclophosphamide; and (ii) 3 days following treatment with CY, injecting patients with a vaccine containing  $10\text{-}25 \times 10^6$  autologous, irradiated melanoma cells. Berd reports that the vaccine induced a "striking inflammatory response in 11/15 patients, consisting of erythema, swelling, warmth and tenderness around tumor masses." Further, 92% of the patients developed DTH to the DNP-conjugated melanoma cells. The reference states that the "DNP-vaccine seems to induce a degree of anti-melanoma immunity not seen with previously tested immunotherapy."

While Berd (1990) teaches that the patients were injected with the DNP-conjugated melanoma vaccine, Berd does not specifically teach that the injection was intradermal, or that the injection was made to 3 sites on an upper arm or leg.

However, Berd (1988) teaches methods of immunotherapy for human melanoma wherein  $10\text{-}25 \times 10^6$  autologous melanoma cells mixed with BCG are injected intradermally into the three sites on the patients upper arm or legs (see page 340, column 1). Berd (1988) reports that patients receiving CY and the melanoma vaccine



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developed DTH to tumor antigens (page 342, column 2). Three of the patients tested showed complete remission, one partial remission and two had minor responses to the vaccine (page 344, column 2).

According, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have practiced the method of Berd (1990) by injecting the DPN-conjugated melanoma vaccine mixed with BCG intradermally to 3 contiguous sites on the patient's upper arm or leg because as taught by Berd (1988) this is a conventional means for administering the melanoma cancer vaccine and would have provided an effective route of administration.

With respect to the recitation in the claims of "wherein administration of said vaccine induces a delayed-type hypersensitivity (DTH) response against unmodified melanoma cells" it is considered to be a property of the vaccine of Berd that it is capable of inducing a DTH response against unmodified melanoma cells. Given that the vaccine of Berd is identical to the vaccine of the present invention, in the absence of evidence to the contrary, the vaccine of Berd (1990) is expected to function similarly to the present vaccine. Therefore, the resulting method of intradermally injecting the DNP-vaccine of Berd (1990) would have necessarily resulted in a DTH response against unmodified melanoma cells.

Further, Berd (1990) does not teach that the vaccine is mixed with BCG. However, Berd (1988; page 340) teaches mixing the melanoma vaccine with the immunological adjuvant BCG. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have mixed the DNP-

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conjugated melanoma vaccine with the immunological adjuvant BCG in order to have further enhanced the patient's immune response.

With respect to claims 28 and 29, Berd (1990) does not characterize the melanoma patients that were treated with the DNP-conjugated melanoma vaccine and thereby does not specifically teach administering the vaccine to post-surgical melanoma patients or to stage 4 melanoma patients. However, Berd (1988; see, e.g., page 340) teaches administering the melanoma vaccine to patients post-surgically and to patients with extensive metastatic disease. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have administered the DNP- conjugated melanoma vaccine of Berd (1990) to patients post-surgically and to stage 4 melanoma patients in order to have provided an effective means of treatment for those patients most in need of therapy.

With respect to claim 30, Berd (1990) teaches that patients were injected with the DNP-conjugated melanoma vaccine every 4 weeks.

With respect to claim 31, Berd (1990) does not teach that the autologous melanoma cells are cryopreserved. However, Berd (1988; page 340) teaches that the tumor masses are removed from the patient and tumor cells are cryopreserved in liquid nitrogen until needed. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used cryopreserved autologous melanoma cells because this would have provided a more convenient means of administering the therapy since such cells could be frozen and stored and then administered at 4 week intervals.

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5. Claims 26-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Murphy et al (Laboratory Investigation. 1990. 62(1): 70A, abstract #412) in view of Berd (1988).

Murphy teaches a method of treating metastatic melanoma wherein the method comprises: (i) administering to a melanoma patient a low dose of cyclophosphamide; and (ii) 3 days following treatment with CY, injecting patients with a vaccine containing  $10\text{--}25 \times 10^6$  autologous, irradiated melanoma cells mixed with Bacille Calmette-Guerin(BCG). Murphy reports that 7 patients showed clinical regression following treatment.

While Murphy teaches that the patients were injected with the DNP-conjugated melanoma vaccine, Murphy does not specifically teach that the injection was intradermal, or that the injection was made to 3 sites on an upper arm or leg.

However, Berd (1988) teaches methods of immunotherapy for human melanoma wherein  $10\text{--}25 \times 10^6$  autologous melanoma cells mixed with BCG are injected intradermally into the three sites on the patients upper arm or legs (see page 340, column 1). Berd (1988) reports that patients receiving CY and the melanoma vaccine developed DTH to tumor antigens (page 342, column 2). Three of the patients tested showed complete remission, one partial remission and two had minor responses to the vaccine (page 344, column 2).

According, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have practiced the method of Murphy by injecting the DPN-conjugated melanoma vaccine mixed with BCG intradermally to 3 contiguous sites

on the patient's upper arm or leg because as taught by Berd (1988) this is a conventional means for administering the melanoma cancer vaccine and would have provided an effective route of administration.

With respect to the recitation in the claims of "wherein administration of said vaccine induces a delayed-type hypersensitivity (DTH) response against unmodified melanoma cells" it is considered to be a property of the vaccine of Berd that it is capable of inducing a DTH response against unmodified melanoma cells. Given that the vaccine of Murphy is identical to the vaccine of the present invention, in the absence of evidence to the contrary, the vaccine of Murphy is expected to function similarly to the present vaccine. Therefore, the resulting method of intradermally injecting the DNP-vaccine of Murphy would have necessarily resulted in a DTH response against unmodified melanoma cells.

With respect to claims 28 and 29, Murphy does not characterize the melanoma patients that were treated with the DNP-conjugated melanoma vaccine and thereby does not specifically teach administering the vaccine to post-surgical melanoma patients or to stage 4 melanoma patients. However, Berd (1988; see, e.g., page 340) teaches administering the melanoma vaccine to patients post-surgically and to patients with extensive metastatic disease. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have administered the DNP- conjugated melanoma vaccine of Murphy to patients post-surgically and to stage 4 melanoma patients in order to have provided an effective means of treatment for those patients most in need of therapy.

With respect to claim 30, Murphy does not specifically teach that patients were injected with the DNP-conjugated melanoma vaccine every 4 weeks. However, Berd (1988a; page 340) teaches repeating the vaccine treatment every 28 days. The number of vaccine treatments ranged from 1 to 15, with a median of 4 treatments. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have intradermally administered the DNP-conjugated melanoma vaccine every 4 weeks because this would have boosted the response to the vaccine and thereby would have increased the effectiveness of the therapy.

With respect to claim 31, Murphy does not teach that the autologous melanoma cells are cryopreserved. However, Berd (1988; page 340) teaches that the tumor masses are removed from the patient and tumor cells are cryopreserved in liquid nitrogen until needed. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used cryopreserved autologous melanoma cells because this would have provided a more convenient means of administering the therapy since such cells could be frozen and stored and then administered at 4 week intervals.

6. Claims 2 and 21-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berd et al (1989) in view of Berd (1988), as applied to claims 26-31 above, and further in view of Fujiwara (The Journal of Immunology. 1980. 124: 863-869).

The teachings of Berd (1989) and Berd (1988) are presented above. Berd (1989) teaches treating melanoma patients with a hapten conjugated melanoma vaccine, wherein the hapten is dinitrophenyl (DNP). Berd (1989) does not teach treating

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melanoma patients with a hapten conjugated melanoma vaccine wherein the hapten is trinitrophenyl (TNP).

Fujiwara (page 864) teaches conjugating TNP to tumor cells and the use of TNP-conjugated tumor cells to treat tumors. The reference teaches that the TNP-conjugated tumor cells induced enhanced tumor-specific immunity leading to regression of growing tumor when administered following priming with TNP (see abstract and page 868). Fujiwara teaches that the augmented immunity is due to the activity of cytotoxic T cells and T cells essential for tumor rejection.

In view of the teachings of Fujiwara of the effectiveness of TNP-conjugated tumor cells to augment immunity and enhance the tumor rejection response and in view of the known structural similarities between DNP and TNP, the ordinary artisan would have expected that TNP-conjugated melanoma cells could be substituted for DNP-conjugated melanoma cells in order to provide an effective means for treating melanoma. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Berd (1989) so as to have used TNP in place of DNP as the hapten in order to have provided an equally effective vaccine for treating melanoma.

7. Claims 2 and 21-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berd et al (1990) in view of Berd (1988), as applied to claims 26-31 above, and further in view of Fujiwara.

The teachings of Berd (1990) and Berd (1988) are presented above. Berd (1990). Berd (1990) does not teach treating melanoma patients with a hapten conjugated melanoma vaccine wherein the hapten is trinitrophenyl (TNP).

Fujiwara (page 864) teaches conjugating TNP to tumor cells and the use of TNP-conjugated tumor cells to treat tumors. The reference teaches that the TNP-conjugated tumor cells induced enhanced tumor-specific immunity leading to regression of growing tumor when administered following priming with TNP (see abstract and page 868). Fujiwara teaches that the augmented immunity is due to the activity of cytotoxic T cells and T cells essential for tumor rejection.

In view of the teachings of Fujiwara of the effectiveness of TNP-conjugated tumor cells to augment immunity and enhance the tumor rejection response and in view of the known structural similarities between DNP and TNP, the ordinary artisan would have expected that TNP-conjugated melanoma cells could be substituted for DNP-conjugated melanoma cells in order to provide an effective means for treating melanoma. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Berd (1990) so as to have used TNP in place of DNP as the hapten in order to have provided an equally effective vaccine for treating melanoma.

8. Claims 2 and 21-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Murphy in view of Berd (1988), as applied to claims 26-31 above, and further in view of Fujiwara.

The teachings of Murphy and Berd (1988) are presented above. Murphy teaches treating melanoma patients with a hapten conjugated melanoma vaccine, wherein the hapten is dinitrophenyl (DNP). Murphy does not teach treating melanoma patients with a hapten conjugated melanoma vaccine wherein the hapten is trinitrophenyl (TNP).

Fujiwara (page 864) teaches conjugating TNP to tumor cells and the use of TNP-conjugated tumor cells to treat tumors. The reference teaches that the TNP-conjugated tumor cells induced enhanced tumor-specific immunity leading to regression of growing tumor when administered following priming with TNP (see abstract and page 868). Fujiwara teaches that the augmented immunity is due to the activity of cytotoxic T cells and T cells essential for tumor rejection.

In view of the teachings of Fujiwara of the effectiveness of TNP-conjugated tumor cells to augment immunity and enhance the tumor rejection response and in view of the known structural similarities between DNP and TNP, the ordinary artisan would have expected that TNP-conjugated melanoma cells could be substituted for DNP-conjugated melanoma cells in order to provide an effective means for treating melanoma. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Murphy so as to have used TNP in place of DNP as the hapten in order to have provided an equally effective vaccine for treating melanoma.

9. Claims 1 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berd et al (1989) and Fujiwara.



The teachings of Berd (1989) are presented above. Berd (1989) teaches using a hapten conjugated melanoma vaccine to treat melanoma patients, wherein the hapten is dinitrophenyl (DNP). Berd (1989) does not teach a hapten conjugated melanoma vaccine wherein the hapten is trinitrophenyl (TNP).

Fujiwara (page 864) teaches conjugating TNP to tumor cells and the use of TNP-conjugated tumor cells to treat tumors. The reference teaches that the TNP-conjugated tumor cells induced enhanced tumor-specific immunity leading to regression of growing tumor when administered following priming with TNP (see abstract and page 868). Fujiwara teaches that the augmented immunity is due to the activity of cytotoxic T cells and T cells essential for tumor rejection.

In view of the teachings of Fujiwara of the effectiveness of TNP-conjugated tumor cells to augment immunity and enhance the tumor rejection response and in view of the known structural similarities between DNP and TNP, the ordinary artisan would have expected that TNP-conjugated melanoma cells could be substituted for DNP-conjugated melanoma cells in order to provide an effective means for treating melanoma. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Berd (1989) so as to have used TNP in place of DNP as the hapten in order to have provided an equally effective vaccine for treating melanoma.

With respect to newly added claim 32, Berd teaches that the hapten-conjugated vaccine is administered with BCG, which is considered to be an immunomodulating drug, since BCG stimulates the immune response. It is noted that the claims do not

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require that the immunomodulating agent is distinct from the immunological adjuvant, and therefore the present claims include vaccines comprising BCG which acts as an immunological adjuvant and immunomodulating drug.

10. Claim 1 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berd et al (1990) and Berd (1998) in view of Fujiwara.

The teachings of Berd are presented above. In particular, Berd (1990) teaches using a hapten conjugated melanoma vaccine to treat melanoma patients, wherein the hapten is dinitrophenyl (DNP). Berd (1990) does not teach a hapten conjugated melanoma vaccine wherein the hapten is trinitrophenyl (TNP).

Fujiwara (page 864) teaches conjugating TNP to tumor cells and the use of TNP-conjugated tumor cells to treat tumors. The reference teaches that the TNP-conjugated tumor cells induced enhanced tumor-specific immunity leading to regression of growing tumor when administered following priming with TNP (see abstract and page 868). Fujiwara teaches that the augmented immunity is due to the activity of cytotoxic T cells and T cells essential for tumor rejection.

In view of the teachings of Fujiwara of the effectiveness of TNP-conjugated tumor cells to augment immunity and enhance the tumor rejection response and in view of the known structural similarities between DNP and TNP, the ordinary artisan would have expected that TNP-conjugated melanoma cells could be substituted for DNP-conjugated melanoma cells in order to provide an effective means for treating melanoma. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Berd (1990) so as to have used

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TNP in place of DNP as the hapten in order to have provided an equally effective vaccine for treating melanoma.

With respect to newly added claim 32, Berd (1988) teaches administering the hapten-conjugated vaccine to enhance the patient's immune response. BCG is considered to be an immunomodulating drug, since BCG stimulates the immune response. It is also noted that the claims do not require that the immunomodulating agent is distinct from the immunological adjuvant, and therefore the present claims include vaccines comprising BCG which acts as an immunological adjuvant and immunomodulating drug.

11. Claims 1 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Murphy in view of Fujiwara.

The teachings of Murphy are presented above. Murphy teaches using a hapten conjugated melanoma vaccine mixed with BCG to treat melanoma patients, wherein the hapten is dinitrophenyl (DNP). Murphy does not teach a hapten conjugated melanoma vaccine wherein the hapten is trinitrophenyl (TNP).

Fujiwara (page 864) teaches conjugating TNP to tumor cells and the use of TNP-conjugated tumor cells to treat tumors. The reference teaches that the TNP-conjugated tumor cells induced enhanced tumor-specific immunity leading to regression of growing tumor when administered following priming with TNP (see abstract and page 868). Fujiwara teaches that the augmented immunity is due to the activity of cytotoxic T cells and T cells essential for tumor rejection.

In view of the teachings of Fujiwara of the effectiveness of TNP-conjugated tumor cells to augment immunity and enhance the tumor rejection response and in view of the known structural similarities between DNP and TNP, the ordinary artisan would have expected that TNP-conjugated melanoma cells could be substituted for DNP-conjugated melanoma cells in order to provide an effective means for treating melanoma. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Murphy so as to have used TNP in place of DNP as the hapten in order to have provided an equally effective vaccine for treating melanoma.

With respect to newly added claim 32, Murphy teaches that the hapten-conjugated vaccine is administered with BCG, which is considered to be an immunomodulating drug, since BCG stimulates the immune response. It is noted that the claims do not require that the immunomodulating agent is distinct from the immunological adjuvant, and therefore the present claims include vaccines comprising BCG which acts as an immunological adjuvant and immunomodulating drug.

## **12. RESPONSE TO ARGUMENTS:**

**Rejections under 35 U.S.C. 103 of claims 26-31 as unpatentable over Berd (1989) in view of Berd (1988), Berd (1990) in view of Berd (1988), and Murphy (1990) in view of Berd (1988).**

In the response of July 5, 2006, Applicants argue that Berd (1989), Berd (1990) and Murphy (1990) are each directed to methods of treating melanoma using haptenized tumor cells as a vaccine, whereas Berd (1988) is directed to methods of

treating melanoma using non-haptenized tumor cells as a vaccine. Applicants argue that "there is nothing in any of these references that would teach or suggest to a skilled person that use of haptenized cells would work in combination with the method disclosed in Berd 1988 as an effective treatment for melanoma."

Applicants arguments have been fully considered but are not persuasive. As discussed previously, the disclosed methods of Berd (1989), Berd (1990) and Murphy (1990) differ from the claimed invention in that they do not specify the location at which the vaccine is injected into the patient, and particularly do not specify injection of the vaccine intradermally at 3 sites on the patients upper arm or leg. However, injection of vaccines intradermally at 3 sites on the patients upper arm or leg was conventional in the art at the time the invention was made. Berd (1988) was cited for teaching this routine mode of administration of vaccines for the treatment of melanoma. The skilled artisan would have clearly recognized that the teachings of Berd (1988) regarding the administration of non-haptenized vaccines would also be applicable to haptenized vaccines given the conventionality of this route of administration of vaccines, particularly for the treatment of melanoma. Applicants have not shown any unexpected results associated with administering the haptenized vaccine intradermally at 3 sites on the patients upper arm or leg and have not provided any sound scientific arguments to support their contention that the teachings of Berd regarding the route of administration of vaccines would not be applicable to haptenized vaccines.

Further, for the purposes of combining references, those references need not explicitly suggest combining teachings much less specific references, In re Nilseen, 851

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F. 2d 1401, 7 USPQ2d 1500 (Fed Cir. 1988). As stated in Ex parte Levengood, 28 USPQ2d 1300, "In order to establish a *prima facie* case of obviousness, it is necessary for the examiner to present *evidence*, preferably in the form of some teaching, suggestion, incentive or inference in the applied prior art, or in the form of generally available knowledge, that one having ordinary skill in the art would have been led to combine the relevant teachings of the applied references in the proposed manner to arrive at the claimed invention". Motivation for combining the teachings of the various references need not be explicitly found in the references themselves, but may be provided by the examiner based on logic and sound scientific reasoning. In the present situation, given the conventionality in the art of administering melanoma vaccines intradermally at 3 sites on the patients upper arm or leg and the specific teachings of Berd to administer melanoma vaccines in this manner, it is maintained that the combined references provide both the motivation and more than a reasonable expectation of success of treating melanoma patients by administering the haptenized vaccines of Berd (1989 and 1990) and Murphy (1990) intradermally at 3 sites on the patients upper arm or leg.

**Rejections under 35 U.S.C. 103 of claims 2 and 21-25 as unpatentable over Berd (1989) in view of Berd (1988) and Fujiwara, and over Berd (1990) in view of Berd (1988) and Fujiwara**

Applicants traverse the 35 U.S.C. 103 rejections of claims 2 and 21-25 over Berd (1989) in view of Berd (1988) and Fujiwara and over Berd (1990) in view of Berd (1988) and Fujiwara by stating that there is no motivation to combine the stated references and

there is no expectation of success in treatment of melanoma with a TNP-modified vaccine. Applicants assert that Berd 1988, 1989 and 1990 disclose methods of treating melanoma using DNP-modified human melanoma cells, while Fujiwara relates only to TNP-modified mouse leukemia or plasmacytoma cells.

Applicant's argument have been fully considered but are not persuasive. While Fujiwara exemplifies methods of vaccination using TNP-conjugated tumor cells to treat mouse leukemia or plasmacytoma, the teachings of Fujiwara are not in fact limited to only the treatment of these two types of cancer. Rather, Fujiwara teaches, in general, that TNP-conjugated tumor cells generate an immune response and enhance the rejection of tumor cells. Fujiwara (abstract) states "The magnitude of tumor-neutralizing activity developed in the presence of TNP-amplifier system was as much as 20-fold greater than for control, and this augmented tumor-neutralizing activity was also tumor specific and T cell mediated. Thus, the present system provides an effective manipulation for eliciting enhanced in vivo tumor rejection as well as in vigor cytotoxic response, and illustrates a role of amplifier T cells in augmentation of syngeneic tumor immunity."

Applicants argue that Fujiwara does not provide any data to show that the treatment can be performed with other types of tumor cells. However, there is no requirement for the reference to provide data to show that the method can be used with other types of tumors. Given the teachings of Fujiwara that the method can be used with 2 types of cancers and the statements that other types of cancers can be treated, one of ordinary skill in the art would have had more than a reasonable expectation of success of using the TNP-conjugated tumor cells to treat other types of tumors. Obviousness does not require absolute predictability but only the reasonable expectation of success. See In re Merck and Company Inc., 800 F. 2d 1091, 231 USPQ 375 (Fed. Cir. 1986)

and In re O'Farrell, 7 USPQ2d 1673 (Fed. Cir. 1988). Additionally, the teachings of Fujiwara do in fact provide the motivation to combine the cited references because Fujiwara teaches that TNP-conjugated tumor cells provide the advantage of augmenting immunity and enhancing the tumor rejection response.

Applicants also traverse this rejection by stating that the method of Fujiwara includes a step of priming by administering TNP modified proteins in order to elicit a stronger response, but that the methods of Berd (1988, 1989 and 1990) do not require this priming step. This argument is not persuasive because the claims do not exclude including a priming step with TNP modified proteins. Further, Fujiwara teaches including the priming step only to further improve the immune response, but does not teach that this step is mandatory. Additionally, Berd (1989 and 1990) do in fact include a priming step with the hapten in which patients are sensitized to DNP by topical administration of dinitrochlorobenzene prior to administering the hapten-conjugated vaccine.

Further, in view of the high level of structural similarity between the DNP and TNP haptens, the ordinary artisan would have expected that TNP could be used in place of DNP and would be equally effective at enhancing the immune response. It is noted that the present specification does not provide any data for TNP-conjugated melanoma vaccines or AED-conjugated melanoma vaccines. The teachings in the specification regarding TNP and AED are limited to a single sentence of: "Other useful haptens include TNP and AED which may be chemically linked to the tumor cells" (see column 3, lines 58-59 of '551). In addressing the enablement of the present invention, **Applicants previously argued in the March 6, 1992 response of '551 that "Other**



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**haptens of the claimed invention, trinitrophenyl and N-iodoacetyl-N'-(5 sulfonic 1-naphthyl) ethylene diamine, would be expected to behave similarly to DNP”** and conclude that the selection and use of alternative haptens, such as TNP, would have been well within the skill of the art. The specification has not established any unexpected results associated with the use of TNP and has acknowledged the obviousness of using alternative haptens with the expectation that they will behave similarly to DNP. Thereby, the claimed invention would have been obvious to and well within the ordinary skill of the art at the time the invention was made. The ordinary artisan also recognizing the similarity in structure between DNP and TNP and appraised of the teachings of Fujiwara of the use of TNP as a hapten to augment the immune response to tumors, would have been motivated to have used, and would have had more than a reasonable expectation of success at using TNP-conjugated melanoma vaccines for the treatment of melanoma.

Therefore, the rejections are maintained because the combined references when considered as a whole provide both the motivation and a reasonable expectation of success of using TNP-conjugated melanoma vaccines in place of DNP-conjugated melanoma vaccines for the treatment of cancer.

**Rejections under 35 U.S.C. 103 of claims 2 and 21-25 as unpatentable over Murphy (1990) in view of Berd (1988) and Fujiwara**

Applicants traverse this rejection by stating that neither Murphy nor Berd teach the use of TNP-modified tumor cells. It is also argued that Fujiwara does not teach using TNP-modified human melanoma cells to treat human melanoma.

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Applicant's argument has been fully considered but is not persuasive. Regarding the Fujiwara reference, Applicants arguments are the same as those presented above. Accordingly, the response to those arguments presented above apply equally to the present grounds of rejection. Further, it is pointed out that the rejection is based on the combined teaches of Murphy (1990), Berd (1988) and Fujiwara, and not on each of the references when taken alone. Fujiwara was not cited for teaching using TNP-modified human melanoma cells to treat human melanoma. Rather, Fujiwara was cited for the general concept of using TNP-modified tumor cells as a vaccine. In view of the teachings of Fujiwara of the effectiveness of TNP-conjugated tumor cells to augment immunity and enhance the tumor rejection response and in view of the known structural similarities between DNP and TNP, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used TNP-conjugated melanoma cells in place of DNP-conjugated melanoma cells in order to have provided an effective means for treating melanoma.

**Rejections under 35 U.S.C. 103 of claims 1 and 32 as unpatentable over Berd (1989) in view of Fujiwara, over Berd (1990) in view of Fujiwara and over Murphy (1990) in view of Fujiwara**

In the response, Applicants traverse this rejection by stating that Fujiwara does not teach using haptenized melanoma cells to treat melanoma. It is argued that there is no motivation to combine the cited references and no reasonable expectation of success.

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These arguments have been fully considered but are not convincing. Again, Fujiwara was not cited to for teaching the use of haptenized melanoma cells to treat melanoma. Rather, Fujiwara was cited for teaching the general concept of using TNP-modified tumor cells to treat tumors. Berd (1989), Berd (1990) and Murphy each was cited for providing the necessary teachings of methods of using haptenized-human melanoma cells to treat human melanomas. Also, the teachings of Fujiwara do in fact provide the motivation to combine the cited references because Fujiwara teaches that TNP-conjugated tumor cells provide the advantage of augmenting immunity and enhancing the tumor rejection response.

Further, it is again pointed out that while Fujiwara exemplifies methods of vaccination using TNP-conjugated tumor cells to treat mouse leukemia or plasmacytoma cells, the teachings of Fujiwara are not in fact limited to only the treatment of these two types of cancer.

Additionally, given the high level of structural similarity between the DNP and TNP haptens, the ordinary artisan would have had more than a reasonable expectation of success of using TNP in place of DNP. Applicants specification and previous arguments support the conclusion that TNP is an obvious variant of DNP. The present specification does not provide any data for TNP-conjugated melanoma vaccines or AED-conjugated melanoma vaccines and Applicants have clearly not established any improved, or unexpected results obtained when using TNP in place of DNP. The teachings in the specification regarding TNP and AED are limited to a single sentence of: "Other useful haptens include TNP and AED which may be chemically linked to the

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tumor cells" (see column 3, lines 58-59 of '551). In addressing the enablement of the present invention, Applicants previously argued in the March 6, 1992 response of '551 that "Other haptens of the claimed invention, trinitrophenyl and N-iodoacetyl-N'-(5 sulfonic 1-naphthyl) ethylene diamine, would be expected to behave similarly to DNP" and conclude that the selection and use of alternative haptens, such as TNP, would have been well within the skill of the art. The specification has not established any unexpected results associated with the use of TNP and has acknowledged the obviousness of using alternative haptens with the expectation that they will behave similarly to DNP. Accordingly, the ordinary artisan also recognizing the similarity in structure between DNP and TNP and the ordinary artisan apprised of the teachings of Fujiwara of the use of TNP as a hapten to augment the immune response to tumors, would have been motivated to have used, and would have had more than a reasonable expectation of success at using TNP-conjugated melanoma vaccines for the treatment of melanoma.

Therefore, the rejections are maintained because the combined references when considered as a whole provide both the motivation and a reasonable expectation of success of using TNP-conjugated melanoma vaccines in place of DNP-conjugated melanoma vaccines for the treatment of cancer.

### ***Double Patenting***

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA

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1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 1 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 47, 65-67, 69-72, 74-77 of copending Application No. 08/203,004. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of '004 recite a method of treatment using a composition comprising each of the components of the presently claimed vaccine. In particular, the claims of '004 recite a method using a composition comprising autologous melanoma cells conjugated to a hapten, and mixed with an immunological adjuvant, wherein the hapten is TNP or AED and the adjuvant is BCG. The claims of '004 recite that the cells have been rendered incapable of growing in the body of a human upon rejection therein, whereas the present claims specify that the cells are irradiated. However, the specification of '004 (page 12) states that "(t)umor cells or extracts are irradiated at 2500 cGy to prevent the cells from growing after injection." Since the claims of '004 are read in light of the specification, it is clear that the claims of '004 encompass irradiated melanoma cells. Accordingly, the claims of '004 disclose a composition comprising each of the components of the presently claimed vaccine and thereby render the presently claimed vaccine obvious.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

**Response to Arguments:**

In the response filed July 5, 2006, Applicants did not specifically address this rejection. Accordingly, the rejection is maintained for the reasons stated above.

14. Claims 2 and 21-32 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 47, 65-72, 74-77 of copending Application No. 08/203,004 in view of Berd (1988). Although the conflicting claims are not identical, they are not patentably distinct from each other because both the present claims and the claims of '004 recite vaccines and a method of treatment using a vaccine, wherein the vaccine comprises autologous melanoma cells conjugated to a hapten, and mixed with the immunological adjuvant. In particular, the hapten is DNP, TNP or AED and the adjuvant is BCG (i.e., an immunomodulating agent). The present claims and the claims of '004 also both encompass methods in which the cyclophosphamide is administered to the patient prior to administering the melanoma vaccine. The claims of '004 recite that the cells have been rendered incapable of growing in the body of a human upon rejection therein, whereas the present claims specify that the cells are irradiated. However, the specification of '004 (page 12) states that "(t)umor cells or extracts are irradiated at 2500 cGy to prevent the cells from growing after injection." Since the claims of '004 are read in light of the specification, it is clear that the claims of '004 encompass irradiated melanoma cells. The claims of '004 differ from the present claims in that they do not recite that the

vaccine is injected intradermally or that the injection was made to 3 sites on an upper arm or leg.

However, Berd (1988) teaches methods of immunotherapy for human melanoma wherein  $10\text{-}25 \times 10^6$  autologous melanoma cells mixed with BCG are injected intradermally into three sites on the patients upper arm or legs (see page 340, column 1). Berd reports that patients receiving CY and the melanoma vaccine developed DTH to tumor antigens (page 342, column 2). Three of the patients tested showed complete remission, one partial remission and two had minor responses to the vaccine (page 344, column 2). According, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have practiced the method of '004 by injecting the hapten conjugated melanoma vaccine mixed with BCG intradermally to 3 contiguous sites on the patient's upper arm or leg because as taught by Berd (1988) this is a conventional means for administering the melanoma cancer vaccine and would have provided an effective route of administration.

With respect to claims 24, 25, 28 and 29, the claims of '004 do not specifically recite administering the vaccine to post-surgical melanoma patients or to stage 4 melanoma patients. However, Berd (1988; see, e.g., page 340) teaches administering melanoma vaccines to patients post-surgically and to patients with extensive metastatic disease. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have administered the hapten-conjugated melanoma to patients post-surgically and to stage 4 melanoma patients in order to have provided an effective means of treatment for those patients most in need of therapy.

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With respect to claim 30, the claims of '004 do not specifically recite administering the vaccine every 4 weeks. However, Berd (1988; page 340) teaches repeating the vaccine treatment every 28 days, for up to 15 cycles of administration. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have intradermally administered the hapten-conjugated melanoma vaccine every 4 weeks because this would have boosted the response to the vaccine and thereby would have increased the effectiveness of the therapy.

With respect to claims 21, 22 and 31, the claims of '004 do not recite that the melanoma cells are cryopreserved. However, Berd (1988; page 340) teaches that the tumor masses are removed from the patient and tumor cells are cryopreserved in liquid nitrogen until needed. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used cryopreserved autologous melanoma cells in the method and compositions of '004 because this would have provided a more convenient means of administering the therapy since such cells could be frozen and stored and then administered at 4 week intervals.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

**Response to Arguments:**

In the response filed July 5, 2006, Applicants did not specifically address this rejection. Accordingly, the rejection is maintained for the reasons stated above.



15. Claims 32 and 33 are rejected under 35 U.S.C. 251 as being based upon new matter added to the patent for which reissue is sought. The added material which is not supported by the prior patent is as follows:

The specification as originally filed does not appear to provide basis for the recitation in newly added claims 32 and 33 of a vaccine which further comprises an immunomodulating drug, particularly wherein the drug is IL-2.

In the response of November 18, 2005, Applicants point to col. 4, lines 4 and 5 of patent 5,290,551 as providing support for this amendment. However, the '551 patent states that "It has been found that administration of an immunomodulating drug, such as IL2, further enhances the efficacy of the present invention. In this embodiment, IL2 is given following the vaccine injection." Accordingly, the '551 patent provides support for the concept of administering the vaccine and then separately administering an immunomodulating drug, such as IL2. However, the '551 patent does not provide support for the concept of a vaccine which contains each of the hapten-conjugated melanoma cells, BCG and an immunomodulating drug such as IL-2.

**Response to arguments:**

In the response filed July 5, 2006, Applicants did not specifically address this rejection. Accordingly, the rejection is maintained for the reasons of record.

16. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 32 and 33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The specification as originally filed does not appear to provide basis for the recitation in newly added claims 32 and 33 of a vaccine which further comprises an immunomodulating drug, particularly wherein the drug is IL-2.

In the response of November 18, 2005, Applicants point to col. 4, lines 4 and 5 of patent 5,290,551 as providing support for this amendment. However, the '551 patent states that "It has been found that administration of an immunomodulating drug, such as IL2, further enhances the efficacy of the present invention. In this embodiment, IL2 is given following the vaccine injection." Accordingly, the '551 patent provides support for the concept of administering the vaccine and then separately administering an immunomodulating drug, such as IL2. However, the '551 patent does not provide support for the concept of a vaccine which contains each of the hapten-conjugated melanoma cells, BCG and an immunomodulating drug such as IL-2.

**Response to arguments:**

In the response filed July 5, 2006, Applicants did not specifically address this rejection. Accordingly, the rejection is maintained for the reasons stated above.

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17. Applicant is reminded of the continuing obligation under 37 CFR 1.178(b), to timely apprise the Office of any prior or concurrent proceeding in which Patent No. 5,290,551 is or was involved. These proceedings would include interferences, reissues, reexaminations, and litigation.

18. Applicant is notified that any subsequent amendment to the specification and/or claims must comply with 37 CFR 1.173(b).

Applicant is further reminded of the continuing obligation under 37 CFR 1.56, to timely apprise the Office of any information which is material to patentability of the claims under consideration in this reissue application.

These obligations rest with each individual associated with the filing and prosecution of this application for reissue. See also MPEP §§ 1404, 1442.01 and 1442.04.

19. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not

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mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (571) 272-0747. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)-272-0735.

The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866)-217-9197 (toll-free).

Carla Myers  
August 1, 2006

  
CARLA J. MYERS  
PRIMARY EXAMINER